

US JAB 948

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of)
François <i>et al.</i>) Examiner J. Reamer
Serial No. 08/604,950)
filed February 22, 1996) Art Unit 1205
for Oral Formulations of an Antifungal)

JUL 1 1997

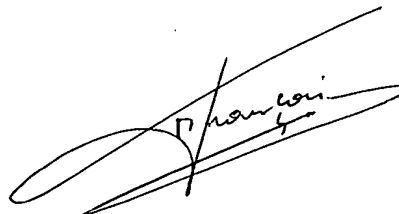
DECLARATION

I, Marc Karel Jozef François, residing at Foxemaatstraat 64, Kalmthout, Belgium make the following declaration :

1. I am a pharmacologist holding a degree from the Free University of Brussels, Belgium, 1974.
2. Since 1982 I am employed at Janssen Pharmaceutica N.V., having its principal place of business at Turnhoutseweg 30, B-2340-Beerse, Belgium as Manager Pharmaceutical Product Development within the Department of Pharmaceutical Development.
3. I am the inventor or co-inventor of several patented inventions in the field of non-solid pharmaceutical formulations, in particular solutions and suspensions of drugs for parenteral or oral administration.
4. The formulations described in the instant application Ser. No. 08/604,950 were prepared and tested under my supervision.

5. I have read the article "Effect of Cyclodextrin on the Pharmacology of Antifungal Oral Azoles" by John S. Hostetler *et al.* in Antimicrobial Agents and Chemotherapy, Feb. 1992, p 477-480, and I confirm that the description of the preparation of the drug formulations for testing is indeed a slight modification of the protocol which we provided to all our investigators working with hydroxypropyl- β -cyclodextrin. The modification resides in the warming up of the solution before the active ingredient is added. The drug formulation is solely adapted for ensuring complete dissolution of the drug, thus allowing the clinical investigators to obtain meaningful pharmacokinetic data on the drug. The drug formulation has a very unpleasant bitter taste because of the dissolved itraconazole and to a lesser extent also because of the propylene glycol. The drug formulation described in the article has a taste which is unacceptable in a commercial product for oral administration.
6. I finally declare that all statements herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Signed, this 19 day of June 1997.

A handwritten signature in black ink, appearing to read "François", with a large, sweeping flourish underneath.

Marc Karel Jozef François